

**REMARKS**

**I. Status of the claims**

Claims 1, 3-21, and 25-41 are the only pending claims in this application. No claim is being amended in this Response.

**II. Claim rejections under 35 U.S.C. § 103(a)**

The Office rejected claims 1, 3-21, and 35-41 under 35 U.S.C. § 103(a) as allegedly being unpatentable over WO 95/13799. Applicants respectfully traverse this rejection.

The Office argues WO 95/13799 teaches "a process for microencapsulating an active agent by coacervation, the process consisting of dissolving a polymer in an organic solvent, which contains the active substance; mixing the polymer/active agent solution (first phase) with another liquid (second phase) to form microdroplets of the active agent encapsulated in the polymer; quenching the mixture at 0-4°C with water or an aqueous solution." Office Action at 2.

The Office states that WO 95/13799 "further discloses the organic solvent [first phase] comprises ethyl acetate and an alcohol or a ketone of 1 to 3 carbon atoms, which includes ethanol and propanol, meeting the requirement of the non-solvent in claims 1 and 41." *Id.*

**A. The Office has not used the proper standard for obviousness**

The Office acknowledges that WO 95/13799 "teaches adding a mixture of ethyl acetate and an alcohol or ketone, instead of adding ethyl acetate first and then the alcohol or ketone." *Id.* at 3. The Office attempts to remedy this deficiency in WO 95/13799 by arguing that "adding a mixture of ingredients has been held prima

facie obvious over adding them sequentially since they would have given substantially the same results." *Id.*

Foremost, Applicants note that the Office has not cited *any* authority in support for this argument. In addition, the Office seems to be improperly employing a *per se* rule to the instant obviousness analysis by applying a court decision here, *without considering the underlying facts in both the decision and the instant case*. "[T]he Federal Circuit [has] held that the use of *per se* rules is improper in applying the test for obviousness under 35 U.S.C. 103." M.P.E.P. § 2116.01. "Rather, 35 U.S.C. 103 requires a highly fact-dependent analysis involving taking the claimed subject matter as a whole and comparing it to the prior art." *Id.*

The new Examination Guidelines for Determining Obviousness under 35 U.S.C. § 103 ("the Obviousness Guidelines") echo the above statements, citing the *Graham* factors as the controlling inquiries in an obviousness analysis and acknowledging that "each case is different and must be decided on its own facts." Fed. Reg. 72(195):57526-57535, 57527, col. 2 (Oct. 10, 2007).

Because the Office has simply referred to an alleged court ruling without considering whether the facts in that ruling can be applied here, the Office has not complied with proper examination procedures.

**B. The Office has misinterpreted relevant case law**

Applicants could not find any court decision that supports application of the Office's proposition that "adding a mixture of ingredients has been held *prima facie*

obvious over adding them sequentially since they would have given substantially the same results," to the instant case.

The relevant case law shows that obviousness could be established where the only difference between a known method and the claimed invention was the order of the method steps, *but only when* such change in the sequence of steps produced the same result as in the prior art method. See, e.g., *Ex parte Rubin*, 128 USPQ 440, 442 (Bd. Pat. App. & Int. 1959) (noting that "appellant concedes that the same product is obtained by either the method claimed herein or that [disclosed in the prior art]" and concluding that "[i]t is evident therefore that no unexpected result is obtained by reversing the order of steps recited in the [prior art]"); *In re Burhans*, 69 USPQ 330 (C.C.P.A. 1946) (not considering Applicant's argument that the order of steps was different in the claimed invention and in the prior art "in the absence of any proof in the record that the order of performing the steps produces any new and unexpected results") (citing *In re Gibson*, 15 USPQ 230 (C.C.P.A. 1930)).

Therefore, if a rule is to be extracted from the above case law that is applicable to the instant facts, it is that in order to find a process obvious over a known process where the only difference is the order of the steps, *the Office first needs to analyze whether changing the order of steps produces the same result as in the prior art*. The Office has not done so here. As will be explained below, the result of the steps disclosed in WO 95/13799 does not produce the same results as in the claimed methods.

**C. The addition of a blend of ethyl acetate and an alcohol or a ketone in WO 95/13799 does not produce the same results as in the claimed invention**

WO 95/13799 recites a process for preparing microparticles comprising, as a first step, preparing a first phase comprising a polymer and an active ingredient dissolved or dispersed in a solvent blend (mutually miscible solvents; *i.e.* a single phase.)

WO 95/13799 at 9; see *also* bottom of 13. The solvent blend may comprise "at least two of the following: an ester, an alcohol, and a ketone." *Id.* at 15. *The end result of this first step is a solution of the polymer in the solvent blend.* *Id.* at 14, line 1.

The Office argues that the solvent blend can comprise ethyl acetate and an alcohol or a ketone having from 1 to 3 carbon atoms. Office Action at 2. The Office further argues that this single step produces the same result as the first two steps recited in instant claim 1. *Id.* It is clear, however, that such is not the case.

Instant claim 1 recites a process for microencapsulating an active principle comprising dissolving a polymer in an organic solvent. Such organic solvent can be, among others, ethyl acetate. See claim 1. The active principle is also present in the organic solvent phase. *Id.* Once the polymer is dissolved in the organic phase, claim 1 recites the step of adding a non-solvent to the solution of polymer, which induces deposition of the polymer on the active principle. *Id.* This step lowers the solubility of the polymer in the organic solvent such that two immiscible phases form: a) the organic solvent, and b) the polymer deposited on the active principle. Specification at 5, lines 1-11. Therefore, *the end result of these two steps is two immiscible phases.*

Contrary to the Office's assertion, the steps disclosed in WO 95/13799 do not produce the same results obtained in the instant invention. In WO 95/13799 a single phase is obtained (with the polymer dissolved therein), whereas in the instant invention two phases are formed, with the polymer forming solid particles. Because the Office's premise is incorrect, and it was the only support for this rejection, the Office has not made a *prima facie* case of obviousness. For at least this reason, Applicants respectfully request that this rejection be withdrawn.

**D. The claimed invention differs from WO 95/13799 in more significant aspects than the sequence of the method steps**

The Office's obviousness analysis alleges that the only difference between the claimed invention and WO 95/13799 is the difference in the order of steps. Office Action at 4. The Office further argues that "the use of one process over the other would have been determined through routine experimentation and dependent upon user's preference." *Id.* Applicants respectfully disagree.

The present invention would not result from optimizing variables in the method disclosed in WO 95/13799. The passages from WO 95/13799 cited by the Office as allegedly suggesting the instant invention relate to a technique commonly known in the art as "solvent extraction." See, e.g., WO 95/13799 at p. 8, lines 14-16; p. 29, lines 4-9. However, the method steps in solvent extraction are not only different from the steps in the instant coacervation method, but, as will be shown below, also have different purposes.

The Office seems to argue that one of ordinary skill in the art could have chosen to use only one of the two solvents required in WO 95/13799's solvent blend (such as

ethyl acetate), to dissolve the polymer in a first step, and then add the second solvent, (such as an alcohol or ketone), in a second and separate step, in order to produce the same result as in the first two recited steps in the claimed invention. Foremost, such proposition is contrary to the requirements taught in WO 95/13799. The reference clearly states that "[t]he solvent system used herein *is a blend of at least two solvents.*" WO 95/13799 at 13, line 28 (italics added). The Office has not explained why one of ordinary skill in the art would use only a single solvent when the reference clearly requires at least two.

However, even if one of ordinary skill in the art ignored this requirement and split the use of the solvents into two separate steps, the end result would not be the formation of two immiscible phases as in the instant invention. See Section II.C above. The result would still be a single phase where the polymer is dissolved. This is because WO 95/13799 teaches that "[t]hese solvents [part of the solvent blend] *must* be:...capable, when blended, of dissolving polymeric matrix material." WO 95/13799 at paragraph bridging 13-14 (italics added). The Office has not explained either why one of ordinary skill in the art would chose not to follow this requirement.

Additionally, in the claimed invention, solid microparticles start to form after the addition of the non-solvent. See, e.g., claim 1. In contrast, the addition of the second immiscible aqueous phase to the first organic phase in WO 95/13799 does not result in the formation of solid microparticles. See, e.g., WO 95/13799 at paragraph bridging 25-26; Examples 1-3. Solid microparticles do not form in WO 95/13799 until after the emulsion of organic solvent/aqueous solution is quenched with a quench liquid. *Id.* See also Attached Annex A.

It is clear, therefore, that the two processes operate under different principles and that the claimed invention would not result from an optimization of the process disclosed in WO 95/13799.

**E. The "composition" disclosed in WO 95/13799 does not contain the same components as in the claimed invention and would not possess inherently the same characteristics**

The Office argues that "since the same chemicals are used in the [WO 95/13799], the composition of the reference would inherently have the same properties." Office Action at 4.

The above statement is incorrect. Although the broad disclosure of WO 95/13799 may teach individual components that could be used in some compositions, and in some steps of the instant invention, WO 95/13799 does not teach the same combination of components, nor their use in the same steps, as in the instant invention.

For example, the Office argues that the same solvent blend of WO 95/13799, capable of comprising ethyl acetate and an alcohol, meets the requirements of both the "organic solvent" and the "non-solvent" of the instant invention.

Such position is mistaken because the claimed method requires that: 1) the organic solvent dissolve the polymer, and 2) the non-solvent "not be a solvent for the polymer." See Claim 1. Therefore, the same solvent (or solvent blend) cannot perform the functions of the "organic solvent" (dissolving the polymer) and the "non-solvent" (not dissolving the polymer) at the same time.

Moreover, as mentioned before, WO 95/13799 requires that each solvent used in the solvent blend "must be:...capable, when blended, of dissolving polymeric matrix material." WO 95/13799 at paragraph bridging 13-14. Thus, the teachings in WO 95/13799 preclude one of ordinary skill in the art from selecting any solvent that could perform the function of the instantly recited "non-solvent."

Additionally, claim 1 currently recites specific pairs of non-solvent and curing agents. The Office has not explained how one of ordinary skill in the art could have arrived at the selection of these specific pairs from the teachings in WO 95/13799 and/or the prior art. Despite this argument, which is made with the sole purpose of advancing prosecution, Applicants reserve the right to pursue the subject matter of instant claim 1 without this limitation.

Therefore, notwithstanding its broad disclosure, WO 95/13799 does not disclose the same compositions as those used in the instant methods.

**F. A proper obviousness analysis shows that WO 95/13799 does not suggest the claimed invention**

The Obviousness Guidelines emphasize analysis of the *Graham* factors as the relevant inquiry when determining obviousness. Fed. Reg. 72(195):57527, col. 2. The guidelines explain that:

[T]he focus when making a determination of obviousness should be on what a person of ordinary skill in the pertinent art would have known at the time of the invention, and on what such a person would have reasonably expected to have been able to do in view of that knowledge.



*Id.* Based on the foregoing remarks, it is clear that the state of the prior art and/or the disclosure in WO 95/13799 would not have led one of ordinary skill in the art to the claimed invention.

For example, WO 95/13799 contains no disclosure regarding a non-solvent that would meet the limitations of claim 1. As mentioned above, the solvent blend component that the Office advances as meeting this limitation would necessarily be a solvent for the polymer, rather than a non-solvent.

Moreover, the methods for the preparation of microparticles in WO 95/13799 and the claimed invention are based on different principles, include different method steps, form solid microparticles at different stages in the process, and are different to such a degree that the disclosure of WO 95/13799 would not have led one of ordinary skill in the art to the instant invention.

Accordingly, Applicants respectfully request that this rejection be withdrawn.

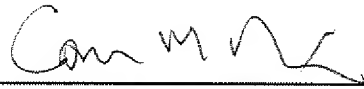
### **III. Conclusions**

In view of the foregoing remarks, Applicants respectfully request the entry of this Amendment and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

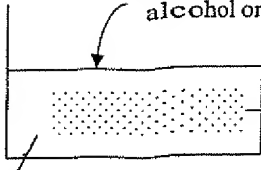
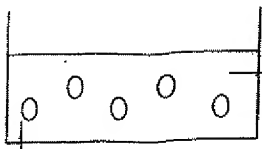
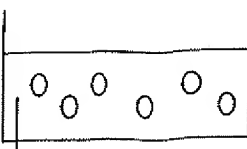
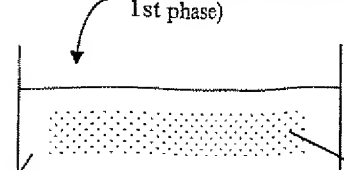
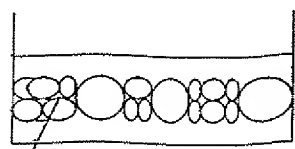
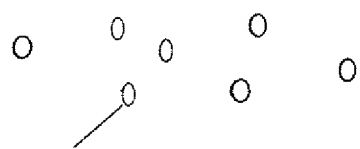
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Dated: October 25, 2007

Attachments: Annex A

# ANNEX A

Our process	WO' 799 "Solvent extraction"
<p>Non-solvent (may be an alcohol or a ketone)</p>  <p>active principle</p> <p>Polymer dissolved in an organic solvent (e.g. ethylacetate)</p> <p>↓ Stirring</p>  <p>one liquid phase only (because the solvent and non-solvent are <u>miscible</u>)</p> <p>Pre-formed <u>solid</u> microparticles (polymer deposited at the surface of the active principle – not dissolved)</p> <p>↓ Addition of curing agent solvent (may be an alcohol or water)</p>  <p>Microparticles <u>cured</u></p>	<p>Second phase (immiscible with the 1st phase)</p>  <p>Active principle</p> <p>First phase (polymer + blend of solvents <u>miscible one to each other</u> "solvent blend" e.g. ethyl acetate <u>and</u> an alcohol or ketone (page 15, lines 9 – 17) + active principle)</p> <p>↓ Emulsion</p>  <p>2 liquid phases <u>immiscible</u> =&gt; Emulsion</p> <p><u>Liquid droplets</u> containing the polymer <u>dissolved</u> therein and the active principle</p> <p>↓ Aqueous extraction with a <u>quench liquid</u></p>  <p>Solid microparticles</p>